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## QUESTION 2: What surface properties favor biofilm formation?

**RESPONSE:** The attachment of bacteria to implant and biological surfaces is a complex process, starting with the initial conditioning film. Roughness, hydrophobicity/hydrophilicity, porosity, pore topology and other surface conditions are the key factors for microbial adhesion. Because of the huge variety of these factors, most of the studies directed at bacterial attachment to the implant surface were limited to specific surface conditions since it is difficult to examine the plethora of parameters concomitantly. There are variable conclusions among the available basic science and animal studies relevant to this topic, many of which will be described in greater detail below. Bacteria can form biofilm on almost all prosthetic surfaces and biological surfaces. To date, this consensus group knows of no surface that is inimicable to the growth of biofilm in vivo.

**LEVEL OF EVIDENCE:** Strong

**DELEGATE VOTE:** Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

### PRE-MEETING RATIONALE

Bacterial biofilms are widely known to contribute to the etiology of chronic infections and implant-associated infections. Biofilm development commences upon formation of a conditioning layer conducive to bacterial attachment, the attachment itself and secretion of a slime-like substance [1]. It is this secretion that enables biofilm formation and ultimately introduces antibiotic resistance and resistance to the host immune system. Several surface properties have been identified that can influence biofilm formation, these include: surface chemistry and functional groups, surface free energy and level of hydrophilicity/hydrophobicity, surface charge, micro- and nano-topography and porosity. Surface chemical composition, micro-roughness and surface free energy would appear to prevail for importance [2].

There is strong evidence that the initial attachment of bacterial species to the surface of a biomaterial is influenced by the presence of adsorbed proteins [1,3]. Wagner et al. [1] found that titanium surfaces preconditioned through exposure to blood plasma enhanced bacterial adhesion for both *Pseudomonas aeruginosa* and *Staphylococcus aureus (S. aureus)*. Likewise, a study performed by Frade et al. presented similar findings with respect to surface adhesion of *Candida albicans* (*C. albicans*) and subsequent biofilm formation on multiple surfaces after serum coating, including polycarbonate, polystyrene, stainless steel, Teflon, polyvinyl chloride and hydroxyapatite [3].

Similarly, there is also strong evidence supporting the conclusion that bacterial adherence and biofilm formation increase with the roughness of the implant surface [4,5]. A study conducted by Karygianni et al. found that *Enterococcus faecalis, S. aureus,* and *C. albicans* adhered more to a rougher implant surface relative to a smoother surface [5]. Furthermore, Braem et al. demonstrated that a porous surface coating was more susceptible to biofilm formation than a smoother titanium-based surface after exposure to *S. aureus* and Staphylococcus epidermidis *Staphylococcus epidermidis* (*S. epidermidis)* [4].

A small number of studies have also examined the impact of the hydrophobicity/ hydrophilicity of implant materials on subsequent biofilm formation [2,3,6]. For example, a study performed by Koseki et al. using *S. epidermidis* showed decreased biofilm formation on cobalt-chromium-molybdenum alloy (Co-Cr-Mo) which was attributed to its increased hydrophobicity [2]. However, two other studies showed contrary results. For instance, *C. albicans* was shown to have less metabolic activity on polycarbonate and stainless steel (hydrophilic surfaces) relative to Teflon (hydrophobic surfaces) [3]. Similarly, some studies contend that hydrophilicity has only trace impact on biofilm formation, as shown by the fact that *S. epidermidis* biofilm formation was not significantly altered by differences in surface wettability [6]. With that, findings remain inconclusive as a whole concerning the impact of implant surface hydrophilicity/hydrophobicity on biofilm formation.

Finally, there are various surface properties that are given moderate recommendations here due to their high-quality evidence but low replication in the studies presented. The first is that surface

nanostructures, such as projections and recesses, reduce overall bacterial adhesion and biofilm formation compared to smooth surfaces [7]. The second is that low nanostructure stiffness inhibits biofilm accumulation, likely due to the susceptibility of these nanostructures to shear forces [8]. The third is that calcium-incorporated oxide coatings on a titanium surface reduces bacterial colonization when compared to non-calcium modified titanium. This is due to calcium drastically decreasing the contact angle [4].

Although there is little consensus in terms of which surface properties are most definitive in contributing to biofilm formation, there are certainly strides in examining the general impact of different properties when considered individually. Due to the complexity of biomaterial properties inherent to orthopaedic implant structure—and the lack of agreement among the literature concluding the impact of these properties—we conclude that biofilm formation is favored by combinations of surface parameters, and so should be assessed as such in the development of biofilm resistant implants. Furthermore, there are few studies examining the impact of surface properties in biofilm formation among human subjects postoperatively and further clinical studies are necessitated.

## REFERENCES


[1] Wagner C, Aytac S, Hänsch GM. Biofilm growth on implants: bacteria prefer plasma coats. Int J Artif Organs. 2011;34:811–8117. doi:10.5301/ijao.5000061.

[2] Koseki H, Yonekura A, Shida T, Yoda I, Horiuchi H, Morinaga Y, et al. Early staphylococcal biofilm formation on solid orthopaedic implant materials: in vitro study. PLoS ONE. 2014;9:e107588. doi:10.1371/journal.pone.0107588.

[3] Frade JP, Arthington-Skaggs BA. Effect of serum and surface characteristics on Candida albicans biofilm formation. Mycoses. 2011;54:e154-162. doi:10.1111/j.1439-0507.2010.01862.x.

[4] Braem A, Van Mellaert L, Mattheys T, Hofmans D, De Waelheyns E, Geris L, et al. Staphylococcal biofilm growth on smooth and porous titanium coatings for biomedical applications. J Biomed Mater Res. A 2014;102:215–224. doi:10.1002/jbm.a.34688.

[5] Karygianni L, Jähnig A, Schienle S, Bernsmann F, Adolfsson E, Kohal RJ, et al. Initial bacterial adhesion on different yttria-stabilized tetragonal zirconia implant surfaces in vitro. Materials (Basel). 2013;6:5659–5674. doi:10.3390/ma6125659.

[6] Subbiahdoss G, Grijpma DW, van der Mei HC, Busscher HJ, Kuijer R. Microbial biofilm growth versus tissue integration on biomaterials with different wettabilities and a polymer-brush coating. J Biomed Mater Res. A 2010;94:533–538. doi:10.1002/jbm.a.32731.

[7] Perera-Costa D, Bruque JM, González-Martín ML, Gómez-García AC, Vadillo-Rodríguez V. Studying the influence of surface topography on bacterial adhesion using spatially organized microtopographic surface patterns. Langmuir. 2014;30:4633–4641. doi:10.1021/la5001057.

[8] Epstein AK, Hochbaum AI, Kim P, Aizenberg J. Control of bacterial biofilm growth on surfaces by nanostructural mechanics and geometry. Nanotechnology. 2011;22:494007. doi:10.1088/0957-4484/22/49/494007.